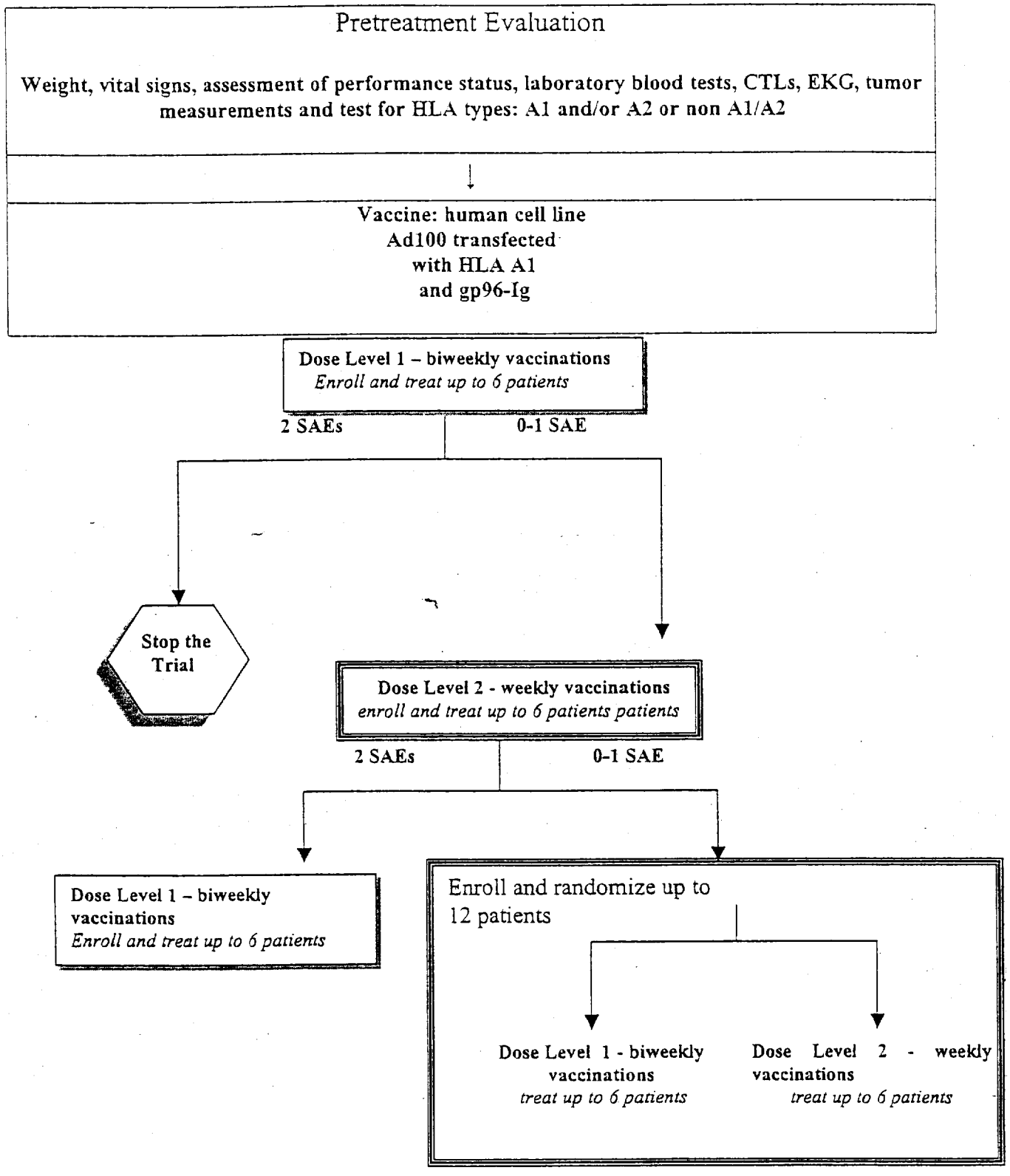
3.1 Research Hypothesis:

Heat Shock protein gp96-Ig is known to increase the immunogenicity and efficacy of tumor vaccines. Irradiated adenocarcinoma cells transfected with gp96-Ig and HLA A1 as tumor vaccines will generate a relatively specific CD8-CTL response without the need for CD4 help. After binding to CD91 on the dendritic cells (DCs) Gp96 peptides are internalized, resulting in the activation of the DCs. Secreted gp96-Ig provides a general pathway through which antigens of cancers cells can be transferred to and cross-presented by dendritic cells (DCs), the professional antigen presenting cells (APCs), to naive T cells in the lymph nodes and induce specific tumor immunity. This response could develop through cross-presentation of shared tumor antigens across the MHC barrier between the patient and the HLA-A1 in vaccine gp96-Ig peptide complexes therefore combines antigenic specificities with adjuvanticity by activating cellular immune response.

3.2 Schema for Study



3.3 Overview of the Study

This is a limited Phase I trial in patients with advanced NSCLC. Allogeneic cultured lung adenocarcinoma cells transfected with HLA A1 and gp96-Ig will be irradiated and injected intradermally into patients suffering from advanced or metastatic non-small cell carcinoma of the lung. Patients will not be matched at the HLA-A locus. Initially six patients will be treated at dose level 1, once every two weeks, 9 injections total. Additional six patients will be treated at the next dose level (weekly vaccinations) with a total of 18 injections, provided toxicity is acceptable at dose level 1. If the toxicity at dose level 2 is acceptable another 12 patients will be treated. They will be randomized six to each dose level.

The immune response in patients will be measured by determining adenocarcinoma specific CD8 CTL precursor frequencies. In all patients, Elispot assay for Interferon-γ (Ifn- γ) will be done to measure cytotoxic function of the CD8 cells. The immunologic response will be correlated with clinical course.

3.3.1 Objectives:

The overall goals are to evaluate the safety and induction of antitumor immune response by administration of a human tumor cell vaccine and correlate with clinical outcome.

The specific objectives are to:

To evaluate the safety and toxicity of administering secretory heat shock protein gp96-Ig transfected allogeneic tumor cell vaccines in advanced NSCLC.

To evaluate whether full allogeneic immunotherapy can elicit tumor cell-specific CD8 CTLs in advanced NSCLC.

Primary endpoint is to examine cellular immune response after an initial course of immunizations.

Secondary endpoint is to examine for responses after subsequent courses of immunizations.